

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:42887 CAPLUS  
DOCUMENT NUMBER: 137:24295  
TITLE: Salts of an isothiazole-4-carboxamide derivative,  
namely 3-(4-bromo-2,6-difluorobenzoyloxy)-5-[3-(4-

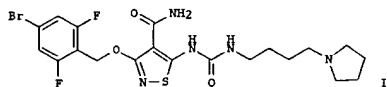
pyrrolidin-1-ylbutyl)ureido]isothiazole-4-carboxylic  
acid amide, and their use as

anti-hyperproliferation

agents  
INVENTOR(S): Gant, Thomas G.; Williams, Glenn Robert  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 38 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044158	A1	20020606	WO 2001-1B2193	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.: US 2000-253513P P 20001128				
GI				

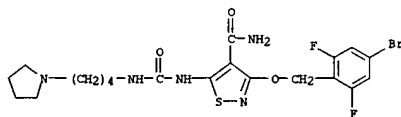


AB The invention relates to the hydrochloride, hydrobromide, hemi-citrate, acetate, p-tosylate, L-tartrate, hemi-succinate, and mesylate salt forms of 3-(4-bromo-2,6-difluoro-benzoyloxy)-5-[3-(4-pyrrolidin-1-

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RN 252003-66-0 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monomethanesulfonate (9CI)  
(CA INDEX NAME)

CH 1

CRN 252003-65-9  
CMF C20 H24 Br F2 N5 O3 S



CH 2

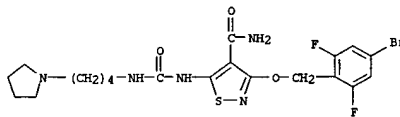
CRN 75-75-2  
CMF C H4 O3 S



RN 252003-71-7 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monohydrochloride (9CI)  
(CA INDEX NAME)

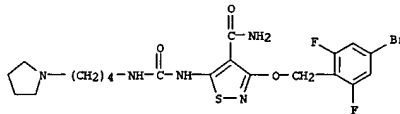
L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)  
ylbutyl)ureido]isothiazole-4-carboxylic acid amide (I). These salts of I are useful in the treatment of various hyperproliferative diseases, including cancers (no data). The invention also relates to pharmaceutical compns. contg. these salts. The invention further relates to methods of treating hyperproliferative diseases, such as cancers, in mammals, esp. humans, by administering the above salts, and to methods of prep. the crystal forms of the salts. For instance, I was dissolved in refluxing EtOH, and the soln. was cooled to ambient temp., treated with 1 equiv HCl (1.0M in Et2O), heated to 50.degree., and cooled at room temp. for 3 days to give 1.HCl in 82% yield. The advantageous properties of all the salts are described in detail; e.g., 1.HCl showed high crystallinity, was hygroscopically stable, and had a low tendency for concd. aq. solns. to form viscous mixts. on standing. Characterizing X-ray powder diffraction spectra are given for I and salts, both as tables and graphical figures.  
IT 252003-66-0P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide mesylate  
252003-71-7P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide hydrochloride (1:1) 433978-97-3P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide hydrobromide (1:1) 433978-98-4P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide hemicitrate 433978-99-5P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide acetate 433979-00-1P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide p-tosylate 433979-01-2P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide L-tartrate 433979-02-3P, 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-(4-(pyrrolidin-1-yl)butyl)ureido]isothiazole-4-carboxylic acid amide hemisuccinate  
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prep. and X-ray powder diffraction spectra of pharmaceutical salts of (bromodifluorobenzoyloxy) [(pyrrolidinylbutyl)ureido]isothiazolecarboxamide for use as antihyperproliferatives)

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 433978-97-3 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monohydrobromide (9CI)  
(CA INDEX NAME)



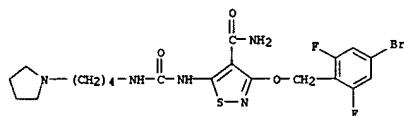
● HBr

RN 433978-98-4 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, 2-hydroxy-1,2,3-propanetricarboxylate (2:1) (9CI) (CA INDEX NAME)

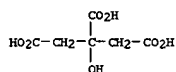
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CRN 252003-65-9  
CMF C20 H24 Br F2 N5 O3 S

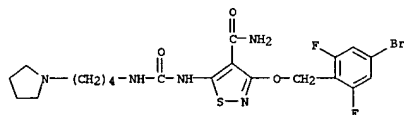
L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)



CH 2  
CRN 77-92-9  
CHF C6 H8 O7

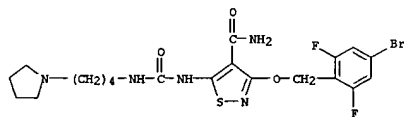


RN 433978-99-5 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino-, monoacetate (9CI) (CA INDEX NAME)  
CH 1  
CRN 252003-65-9  
CHF C20 H24 Br F2 N5 O3 S



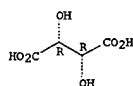
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CRN 64-19-7  
CHF C2 H4 O2

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)

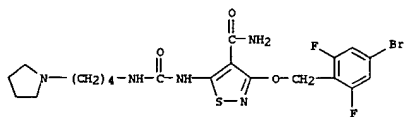


CH 2  
CRN 87-69-4  
CHF C4 H6 O6

Absolute stereochemistry.



RN 433979-02-3 CAPLUS  
CN Butanedioic acid, compd. with  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-4-isothiazolecarboxamide (1:2) (9CI) (CA INDEX NAME)  
CH 1  
CRN 252003-65-9  
CHF C20 H24 Br F2 N5 O3 S



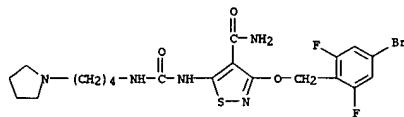
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CRN 110-15-6  
CHF C4 H6 O4

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)

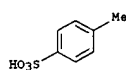


RN 433979-00-1 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CH 1  
CRN 252003-65-9  
CHF C20 H24 Br F2 N5 O3 S



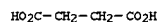
CH 2  
CRN 104-15-4  
CHF C7 H8 O3 S



RN 433979-01-2 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

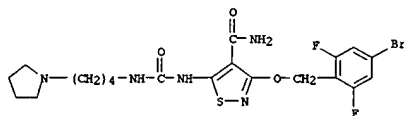
CH 1  
CRN 252003-65-9  
CHF C20 H24 Br F2 N5 O3 S

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 252003-65-9, 3-[(4-bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-yl)butyl]ureido]isothiazole-4-carboxylic acid amide  
RL: FRP (Properties); RCT (Reactant); RACT (Reactant or reagent)  
(prepn. and X-ray powder diffraction spectra of pharmaceutical salts of

(bromodifluorobenzyl)oxy[(pyrrolidinylbutyl)ureido]isothiazolecarboxamide for use as antihyperproliferatives)  
RN 252003-65-9 CAPLUS  
CN 4-isothiazolecarboxamide,  
3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino- (9CI) (CA INDEX NAME)

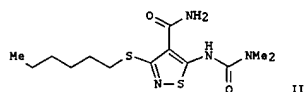
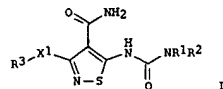


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:784087 CAPLUS  
DOCUMENT NUMBER: 132:22961  
TITLE: Preparation of isothiazolamide urea derivatives  
as  
INVENTOR(S): anticancer agents  
Larson, Eric Robert; Noe, Mark Carl; Gant, Thomas  
George  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 132 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962890	A1	19991209	WO 1999-1B797	19990503
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9933421	A1	19991220	AU 1999-33421	19990503
BR 9910900	A	20010213	BR 1999-10900	19990503
EP 1084114	A1	20010321	EP 1999-914724	19990503
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002517384	T2	20020618	JP 2000-552102	19990503
US 6235764	B1	20010522	US 1999-316837	19990521
ZA 9903752	A	20001204	ZA 1999-3752	19990603
NO 2000006071	A	20001130	NO 2000-6071	20001130
US 2001020034	A1	20010906	US 2001-803296	20010309
PRIORITY APPLN. INFO.: US 1998-87963P P 19980604 WO 1999-1B797 W 19990503 US 1999-316837 A3 19990521				
OTHER SOURCE(S): MARPAT 132:22961 GI				

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)

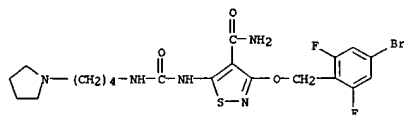


AB Title compds. (I) [X1 = O or S; R1 = H, (un)substituted alkyl, alkenyl, alkynyl, acyl, (CH2)t(hetero)aryl, C(O)(CH2)t(hetero)aryl, etc.; t = 0-5; R2 = R1, SO2(CH2)t(hetero)aryl, etc.; or R1 and R2 taken together with the attached N = 4-10 membered (un)substituted poly- or monocyclic ring or 5-10 membered (un)substituted heteroaryl ring; R3 = H, (un)substituted alkyl, alkenyl, alkynyl, (CH2)t(hetero)aryl, etc.] were prepd. for use in the treatment of hyperproliferative disorders, such as cancer. Thus, 3-(4-cyano-3-mercaptoisothiazol-5-yl)-1,1-dimethylurea (prepn. given) was alkylated with 1-iodohexane (51%) and the product treated with concd. H2SO4 to yield the isothiazolamide (II) (78%). I are inhibitors of receptor tyrosine kinases and bind to or modulate the KDR/FLK-1 receptor (no data) and may be used to treat disorders related to vasculogenesis or angiogenesis.

IT 252003-65-9P 252003-66-0P 252003-71-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (target compd.; prepn. of isothiazolamide urea derivs. as anticancer agents and for the treatment of disorders related to vasculogenesis and/or angiogenesis)

RN 252003-65-9 CAPLUS  
CN 4-Isouthiazolecarboxamide, 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

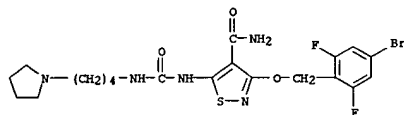
L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 252003-66-0 CAPLUS  
CN 4-Isouthiazolecarboxamide, 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CH 1

CRN 252003-65-9  
CMF C20 H24 Br F2 N5 O3 S



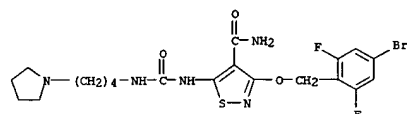
CH 2

CRN 75-75-2  
CMF C H4 O3 S



RN 252003-71-7 CAPLUS  
CN 4-Isouthiazolecarboxamide, 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

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	ENTRY	SESSION
FULL ESTIMATED COST	9.17	224.82
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.24	-1.24

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PASSWORD:

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NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area  
NEWS 4 Apr 09 ZDB will be removed from STN  
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and  
IFIUDB  
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and  
ZCAPLUS  
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available  
NEWS 9 Jun 03 New e-mail delivery for search results now available  
NEWS 10 Jun 10 MEDLINE Reload  
NEWS 11 Jun 10 PCTFULL has been reloaded  
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment  
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;  
saved answer sets no longer valid  
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY  
NEWS 15 Jul 30 NETFIRST to be removed from STN  
NEWS 16 Aug 08 CANCERLIT reload  
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 18 Aug 08 NTIS has been reloaded and enhanced  
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded  
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded  
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced  
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file  
NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS  
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA  
  
NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002  
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NEWS INTER General Internet Information  
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NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
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STRUCTURE FILE UPDATES: 19 SEP 2002 HIGHEST RN 453507-55-6

DICTIONARY FILE UPDATES: 19 SEP 2002 HIGHEST RN 453507-55-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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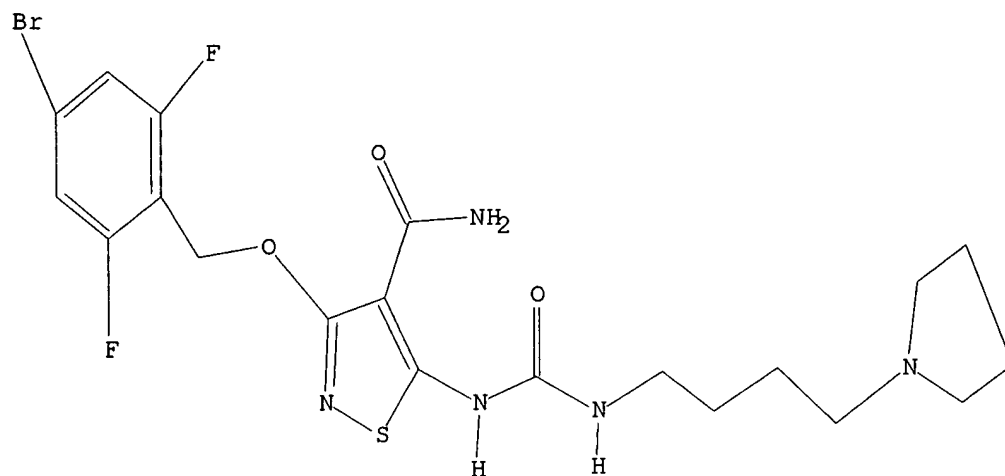
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L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 43 TO ITERATE

100.0% PROCESSED 43 ITERATIONS

10 ANSWERS

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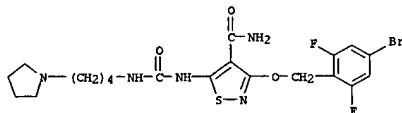
L2 10 SEA SSS FUL L1

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L2 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 433979-02-3 REGISTRY  
 CN Butanedioic acid, compd. with  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-  
 {[(4-(1-pyrrolidinyl)butyl)amino]carbonyl}amino-4-isothiazolecarboxamide  
 (1:2) (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-  
 yl)butyl]ureido]isothiazole-4-carboxylic acid amide hemisuccinate  
 MF C20 H24 Br F2 N5 O3 S . 1/2 C4 H6 O4  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 252003-65-9  
 CMF C20 H24 Br F2 N5 O3 S



CM 2

CRN 110-15-6  
 CMF C4 H6 O4

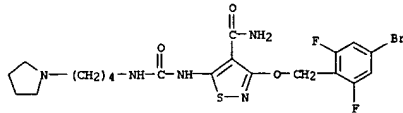
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1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 433979-01-2 REGISTRY  
 CN 4-isothiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-  
 yl)butyl]ureido]isothiazole-4-carboxylic acid amide L-tartrate  
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 LC STN Files: CA, CAPLUS, TOXCENTER

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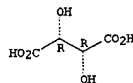
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CM 2

CRN 87-69-4  
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Absolute stereochemistry.

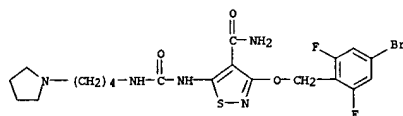


1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 433979-00-1 REGISTRY  
 CN 4-isothiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-  
 yl)butyl]ureido]isothiazole-4-carboxylic acid amide p-tosylate  
 MF C20 H24 Br F2 N5 O3 S . C7 H8 O3 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

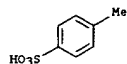
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CM 2

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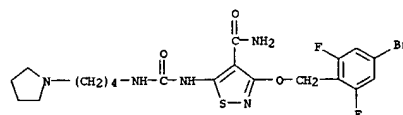


1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 433978-99-5 REGISTRY  
 CN 4-isothiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monoacetate (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-  
 yl)butyl]ureido]isothiazole-4-carboxylic acid amide acetate  
 MF C20 H24 Br F2 N5 O3 S . C2 H4 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

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CRN 252003-65-9  
 CMF C20 H24 Br F2 N5 O3 S



CM 2

CRN 64-19-7  
 CMF C2 H4 O2



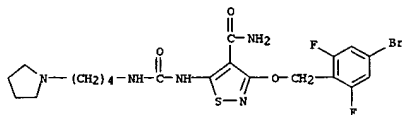
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)



L2 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 433978-98-4 REGISTRY  
 CN 4-Isothiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, 2-hydroxy-1,2,3-propanetricarboxylate (2:1) (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
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 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

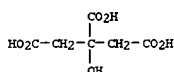
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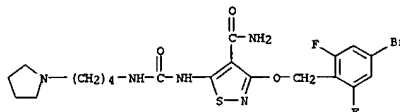
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1 REFERENCES IN FILE CA (1962 TO DATE)  
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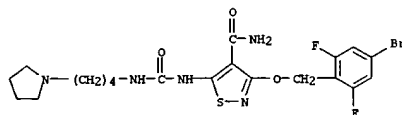
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 RN 433978-97-3 REGISTRY  
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 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monohydrobromide (9CI)  
 (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-yl)butyl]ureido]isothiazole-4-carboxylic acid amide hydrobromide (1:1)  
 MF C20 H24 Br F2 N5 O3 S . Br H  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER  
 CRN (252003-65-9)



● HBr

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 252003-71-7 REGISTRY  
 CN 4-Isouthiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monohydrochloride (9CI)  
 (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-yl)butyl]ureido]isothiazole-4-carboxylic acid amide hydrochloride (1:1)  
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 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
 CRN (252003-65-9)



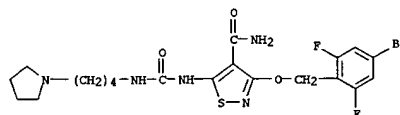
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2 REFERENCES IN FILE CA (1962 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 252003-66-0 REGISTRY  
 CN 4-Isouthiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monomethanesulfonate (9CI)  
 (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-Bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-yl)butyl]ureido]isothiazole-4-carboxylic acid amide mesylate  
 MF C20 H24 Br F2 N5 O3 S . C H4 O3 S  
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CH 1

CRN 252003-65-9  
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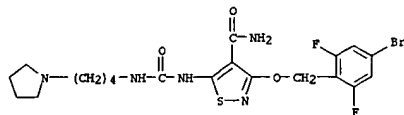
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CRN 75-75-2  
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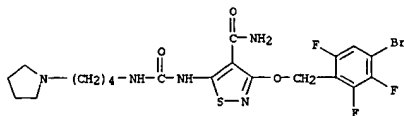
2 REFERENCES IN FILE CA (1962 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2002 ACS  
 RN 252003-65-9 REGISTRY  
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 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[(4-  
 (1-pyrrolidinyl)butyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-[(4-bromo-2,6-difluorobenzyl)oxy]-5-[3-[4-(pyrrolidin-1-  
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 FS 3D CONCORD  
 MF C20 H24 Br F2 N5 O3 S  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*  
 2 REFERENCES IN FILE CA (1962 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L2 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2002 ACS  
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 NAME)  
 FS 3D CONCORD  
 MF C20 H23 Br F3 N5 O3 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*  
 1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	156.46	156.67

FILE 'REGISTRY' ENTERED AT 17:35:04 ON 20 SEP 2002  
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STRUCTURE FILE UPDATES: 19 SEP 2002 HIGHEST RN 453507-55-6  
DICTIONARY FILE UPDATES: 19 SEP 2002 HIGHEST RN 453507-55-6

TSKA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> STR 252003-65-9

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=> S L3 FAM FUL

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FULL SCREEN SEARCH COMPLETED - 19 TO ITERATE

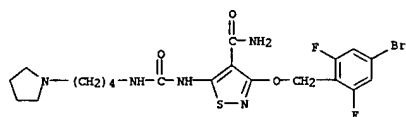
100.0% PROCESSED 19 ITERATIONS 9 ANSWERS  
SEARCH TIME: 00.00.01

L4 9 SEA FAM FUL L3

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=> D SCAN

L4 9 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
 IN 4-Isothiazolecarboxamide,  
 3-[(4-bromo-2,6-difluorophenyl)methoxy]-5-[[[4-(1-pyrrolidinyl)butyl]amino]carbonyl]amino]-, monohydrochloride (9CI)  
 MF C20 H24 Br F2 N5 O3 S . Cl H



● HCl

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s 14 and caplus/lc  
24550097 CAPLUS/LC  
L5 9 L4 AND CAPLUS/LC

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	58.98	215.65

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FILE COVERS 1907 - 20 Sep 2002 VOL 137 ISS 13  
FILE LAST UPDATED: 19 Sep 2002 (20020919/ED)

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L6 2 L5  
  
=> d 1-2 ibib abs hitstr

**SALTS OF A ISOTHIAZOLE-4-CARBOXAMIDE AND THEIR USE AS ANTI-HYPERPROLIFERATION AGENTS**

Patent Number: WO0244158  
Publication date: 2002-06-06  
Inventor(s): WILLIAMS GLENN ROBERT (US); GANT THOMAS G (US)  
Applicant(s): WILLIAMS GLENN ROBERT (US); GANT THOMAS G (US); PFIZER PROD INC (US)  
Requested Patent: ☐ WO0244158  
Application Number: WO2001IB02193 20011119  
Priority Number(s): US20000253513P 20001128  
IPC Classification: C07D275/03; A61K31/427; A61P35/00  
EC Classification: C07D275/02D3  
Equivalents:  
Cited Documents: WO9962890

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**Abstract**

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The invention relates to hydrochloride, hydrobromide, hemi-citrate, acetate, p-tosylate, L-tartrate, hemi-succinate, and mesylate salt forms of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-yl-butyl)-ureido]-isothiazole-4-carboxylic acid amide having the following formula: formula 1. The invention also relates to pharmaceutical compositions containing the hydrochloride, hydrobromide, hemi-citrate, acetate, p-tosylate, L-tartrate, hemi-succinate, and mesylate salts of formula 1. The invention further relates to methods of treating hyperproliferative diseases, such as cancers, in mammals, especially humans by administering the above salts and to methods of preparing the crystal forms of the above salts.

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## INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/IB 01/02193

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D275/03 A61K31/427 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 62890 A (PFIZER PRODUCTS INC.) 9 December 1999 (1999-12-09) the whole document, particularly page 13, lines 1-12, and claim 9, 1st and 8th compound -----	1-20

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

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- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

28 February 2002

Date of mailing of the international search report

06/03/2002

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Allard, M

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

In International Application No  
PCT/IB 01/02193

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9962890	A	09-12-1999	
		AU 3342199 A	20-12-1999
		BG 104998 A	31-07-2001
		BR 9910900 A	13-02-2001
		CN 1303380 T	11-07-2001
		EP 1084114 A1	21-03-2001
		HR 20000835 A1	31-12-2001
		WO 9962890 A1	09-12-1999
		NO 20006071 A	30-11-2000
		PL 344691 A1	19-11-2001
		US 6235764 B1	22-05-2001
		US 2001020034 A1	06-09-2001
		ZA 9903752 A	04-12-2000

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